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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
COOK, LISA V

ART UNIT	PAPER NUMBER
1641	12

DATE MAILED: 04/08/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/035,368	HOEFFLER ET AL.	
	Examiner	Art Unit	
	Lisa V. Cook	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-24 and 48-70* is/are pending in the application.

4a) Of the above claim(s) *19,20 and 51-59* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18,21-24,48-50,55 and 60-70* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *18-24 and 48-70* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3&5* .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicants' species election with traverse of Group V drawn to IgG, IgM, IgE, or IgA antibodies (claims 18, 21-24, 48-50, 55, and 60-70) in Paper #11, filed 1/28/03 is acknowledged. Applicant argues that the while the species of antibodies as set forth are independent and patentably distinct, they all share a commonality of operation, function and effect under MPEP 806.04(e) with respect to the claimed methods. Applicants argument has been carefully considered but not found persuasive for the following reasons:

Once a claim that is determined to be generic is allowed, all of the claims drawn to species in addition to the elected species which include all the limitations of the generic claim will ordinarily be obviously allowable in view of the allowance of the generic claim, since the additional species will depend thereon or otherwise include all of the limitations thereof. When all or some of the claims directed to one of the species in addition to the elected species do not include all the limitations of the generic claim, then that species cannot be claimed in the same case with the other species. See MPEP § 809.02(c)

In other words species restriction for examination is proper and if the method drawing the independent species to a shared commonality of operation, function, and effect is found allowable the addition species will be withdrawn from restriction.

The Restriction Requirement is still deemed proper and is therefore made **FINAL.**

2. Currently, claims 18-24 and 48-70 are subject to Restriction and Election Requirement. Claims 19, 20, 51-54, and 56-59 have been withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as claims drawn to a non-elected invention. Claims 18, 21-24, 48-50, 55, and 60-70 are under consideration.

Priority

3. If applicant desires priority under 35 U.S.C. 119(e) based upon a previously filed copending application, specific reference to the earlier filed application (60/073,605-filed 2/4/98) must be made in the instant application. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph. The status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No._____" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application. Please updated the first line of the specification to include the following: "This application is a divisional of U.S. Serial No. 09/245,615 filed February 4, 1999 (now abandoned)".

4. Parent applications USSN 09/245,615 and USSN 09/245,615 were not available to the examiner at this time. Applicant is invited to verify that the instant claimed methods have written support and enablement under 35 USC 112, first paragraph, for the instant claims to USSN 10/035,368 filed 10/26/01. The instant claims may not have benefit under 35 USC §120 of all the parent filing dates. USSN 09/245,615 claimed microarray devices. If applicant disagrees, applicants should present a detailed analysis as to why the claimed subject matter has clear support in the parent application.

5. The filing date of the instant claims is deemed to be the filing date of the instant application 10/26/01.

Drawings

6. Any drawing corrections requested, but not made in the prior application should be repeated in this application if such changes are still desired. If the drawings were changed and approved during the prosecution of the prior application, a petition may be filed under 37 CFR 1.182 requesting the transfer of such drawings provided the parent application has been abandoned. However, a copy of the drawings as originally filed must be included in the 37 CFR 1.60 application papers to indicate the original content.

Information Disclosure Statement

7. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the examiner on form PTO-892 or applicant on form PTO-1449 have cited the references they have not been considered.

8. The information disclosure statements filed 4/08/02 - Paper#3 and filed 4/23/02 – Paper #5 have been considered as to the merits prior to First Action.

Specification

9. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

I. The use of the trademarks has been noted in this application. (See for example "Invitrogen" page 16 0063, "Texas Red" page 17 0068, "Stratagene page 22 0088). They should be capitalized wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

II. The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973). Please see page 7 section 0029.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 18, 21-24, 48-50, 55, and 60-70 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims 18, 21-24, 48-50, and 60-70 are vague and indefinite because it is not clear as to how the first cell population relates to the second cell population. Because the method is directed to the comparative analysis of protein expression between both the populations, it is not clear how such an assessment can be established if the cell populations are not related in some way. In other words, if the two cell populations are the same and one is exposed to a test compound while the other is not exposed. They can be subjected to comparative analysis. If not such relationship exists they will produced two independent protein patterns having no common link for analysis. Please identify the relationship of the two cell populations to each other in the claims.

B. The terms "resting state and stimulated state" in claim 23 are relative terms which renders the claim indefinite. The terms are not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is suggested that applicants intended meaning with respect to resting and stimulated be outline in the claims to obviate this rejection.

C. In claims 21, 23, and 48-50 the use of the term "derived" is indefinite. As recited it is not clear if Applicant intends to mean the limitation following the term is required or is this to mean any composition will suffice as long as it has the limitation following the term as a parent source. For example in claim 21 is the first cell lysate a normal cell or any cell which starts as a normal cell? The claim could be interpreted to mean the first cell lysate is a normal cell or a cell derived from a normal cell (such as a "abnormal cell" configured as such after normal cell non function). If applicant intends to mean the first cell lysate is a normal cell, the term "derived should be eliminated in order to obviate this rejection.

D. The use of "tissue type" in claims 48-50 is indefinite because it is not clear what the term is to encompass. What limitation does Applicant intend to mean? The cell lysates are from the same tissue, such as the heart. The cell lysates contain a certain tissue type component such as "plasminogen". The term "tissue type" has not been defined in the instant disclosure, therein the metes and bounds of the claims cannot be determined. Please clarify.

E. Claims 55, and 60-63 are indefinite for being in improper Markush format. The office recommends the use of the phrase "selected from the group consisting of...." with the use of the conjunction "and" rather than "or" in listing species. See MPEP 2173.05(h).

Applicant will note that the art rejections are under both 35 USC 102(a) and 102(e) because the priority date of the instant claims is in question.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

I. Claims 18, 21, 23, 24, 48, 49, and 60-62 are rejected under #35 U.S.C. 102(a)(e) as being anticipated by Chin et al. (6,197,599).

Chin et al. teach method to detect proteins (comparing protein expression). An array of antibodies (device comprising multiple immobilized agents for protein detection such as antibodies) is exposed to proteins to monitor the expression and properties of a large number of proteins. See abstract and column 1 line 52 through column 2 line 3. In one embodiment the proteins are metabolically labeled with different radioactive isotopes (S-35 for total proteins – Applicants resting state and P-32 for phosphorylated proteins – Applicants stimulated state). Accordingly, the amount of labeled proteins bound to each antibody on an array can be quantitated by autoradiography and densiometry. Column 5 lines 17. The protein arrays may comprise multiple recombinant proteins (antibodies) to monitor protein-protein interaction therein allowing one to compare protein expression patterns such as the expression in posttranslational modifications between two types of cell, tissue, or patient specimen. Column 5 line 61 through column 6 line 14. Various supports or solid phases are taught. They include glass, plastic, membranes, or microscopic slides. See column 4 lines 9- 22. Example 2 teaches the process of exposing two different cell lysates to two identical arrays and further evaluating the protein expression patterns to evaluate Hela cell transfection. See column 6 –Column 7.

With respect to testing various lystaes as recited in claims 21, 48, and 49, Chin et al. teach that their protein expression method can be utilized to compare protein profiles from different sources, from the same source, further subjected to different conditions.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

I. Claims 22, 50, 63, 69, and 70 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chin et al. (US Patent #6,197,599) in view of James F. Cupo (Journal of Chromatography, 569, 1991, 389-40).

Please see Chin et al. as set forth above.

Chin et al. differ from the instant invention in not teaching protein expression pattern evaluation in cancer diseases or virus cell lines (like T cells) and further allowing for cellular replication distinctions (differential development) via polyacrylamide.

However, Cupo teaches a two-dimensional polyacrylamide gel electrophoresis procedure to measure matrix proteins. The proteins are tissue-type specific and can reflect changes in the state of differentiation of a cell. The method can further distinguish between a diseased cell and a normal cell. The disease states include various cancers, autoimmune disease, and adenoviral infection. See abstract. The method is quick and efficient employing the appropriate antibodies to the protein of interest. Page 403, 1st paragraph. Protein patterning in T lymphocytes (T cells) is outlined on page 400. The method is used to detect early stages of viral infection because a virus must replicate cellular components associated with the nuclear matrix. Such changes are evident in protein patterning analysis. See page 403 – 4.3.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use protein patterning procedures to evaluate cancer diseases or virus cell lines (like T cells) and further allowing for cellular replication distinctions (differential development) via polyacrylamide as taught by Cupo in the high through put protein pattering procedure of Chin et al. because Cupo taught that two-dimensional gels can determine tissue-type specific differences in nuclear matrix proteins and the differences between normal and carcinogenic cells. See page 402 - 4.2 Further these proteins play an important role in cells. Utilization of the proteins can lead to the development of diagnostic agents to detect various diseased conditions of the cell and organism (including cancer and viruses). Cupo page 404.

II. Claim 68 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chin et al. (US Patent #6,197,599) in view of James F. Cupo (Journal of Chromatography, 569, 1991, 389-40).

Please see Chin et al. in view of Cupo as set forth above.

Chin et al. in view of Cupo differ from the instant invention in not specifically teaching the first cell lysate comprising an arterial endothelial cell lysate and the second cell lysate comprising a venous endothelial cell lysate.

However such modification with respect to the type of cells evaluated in the instant method is view as mere design choice and optimization. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to various cells in the methods of Chin et al. in view of Cupo because it would have been an obvious combination of a known cells to evaluate their protein expression via the methods taught by Chin et al. in view of Cupo. The changes in cell type for evaluation are routine optimizations that are almost always determined and used in methods to test the properties of interest.

Unless the result obtained in the instant application is a significant and unexpected difference over the prior art, it would have been prima facie obvious for one of ordinary skill in the art to analyze various cell types\ in the given parameters to determine the unknown as a means of optimizing the methods provided by the art.

III. Claim 55 and 64-67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chin et al. (US Patent #6,197,599) in view of Kauvar (US Patent #5,541,070).

Please see Chin et al. as set forth above.

Chin et al. differ from the instant invention in not teaching immunoglobulin (Ig) antibody binding affinity.

Kauvar teach method of characterizing drugs (proteins) via antibody arrays comprising different binding affinities. The antibody arrays produce characteristic profiles (protein profiles), which can be evaluated or compared to assess the analyte in compound detected. See abstract and figure 5. The antibodies used were mostly of the IgG, IgM forms with vary binding affinity (binding coefficients). See column 8 line 11-14 and figure 2B.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to employ various immunoglobulin antibodies with various affinities as taught by Kauvar in the methods of Chin et al. because Kauvar taught that his invention offered a method of profiling a particular analyte by taking advantage of its specific pattern of reactivity against a panel of antibodies of varying specificity and affinity. Column 3 lines 11-24.

In this method small quantities of analyte can be tested against a large collection of potentially cross reactive antibodies to generate rapid, low cost, data analysis. Column 4 lines 60-67.

13. For reasons aforementioned, no claims are allowed.

Remarks

14. Prior art made of record and not relied upon is considered pertinent to the applicant's disclosure:

Kingsmore et al. (U.S. Patent#6,531,283) teach protein expression profiling techniques.

Fields et al. (U.S. Patent #5,283,173) disclosed systems to measure protein-protein interactions.

15. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 Fax number is (703) 308-4242, which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (703) 305-0808. The examiner can normally be reached on Monday-Friday from 8:00 AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (703) 305-3399.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Lisa V. Cook
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4/2/03

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